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## **Impact of vessel attenuation on quantitative coronary angiography with 64-slice CT**

Husmann, L ; Gaemperli, O ; Valenta, I ; Schepis, T ; Scheffel, H ; Stolzmann, P ; Leschka, S ;  
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**Abstract:** The aim of the study was to determine the impact of vessel attenuation on quantitative 64-slice computed tomography coronary angiography (CTCA). CTCA and invasive quantitative coronary angiography (QCA) were performed in 100 consecutive patients (42 women, 58 men; mean age 64.4+/-9.4 years; age range 39-87 years). In QCA, stenoses were quantified with dedicated software, whereas in CTCA, stenosis severity was assessed with an electronic caliper tool: stenoses were graded in 10% steps and assigned as either a calcified or non-calcified lesion. Vessel attenuation in the left main (LMA) and the proximal right coronary artery (RCA) were measured and correlated with differences in quantifications of stenosis grade between QCA and CTCA. A total of 113 coronary stenoses were detected by both methods (94 significant and 19 non-significant); 52 stenoses were rated as non-calcified and 61 as calcified lesions. The mean difference between QCA and quantitative CTCA grading was 5.1+/-16.9% (range -27 to 46%) overall; 1.9+/-14.2% (range -27 to 38%) for non-calcified lesions and 7.8+/-18.6% (range -23 to 46%) for calcified lesions. Mean vessel attenuation was 362+/-76 HU (range 191 to 584 HU) in the LMA and 333+/-81 HU (range 162 to 564 HU) in the RCA. Attenuation did not significantly correlate with differences in QCA and CTCA gradings; neither overall, nor for calcified or non-calcified lesions. When 64-slice CTCA is used, coronary vessel attenuation had no impact on the quantitative grading of stenoses.

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## Impact of vessel attenuation on quantitative coronary angiography with 64-slice CT

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**ABSTRACT.** The aim of the study was to determine the impact of vessel attenuation on quantitative 64-slice computed tomography coronary angiography (CTCA). CTCA and invasive quantitative coronary angiography (QCA) were performed in 100 consecutive patients (42 women, 58 men; mean age  $64.4 \pm 9.4$  years; age range 39–87 years). In QCA, stenoses were quantified with dedicated software, whereas in CTCA, stenosis severity was assessed with an electronic caliper tool: stenoses were graded in 10% steps and assigned as either a calcified or non-calcified lesion. Vessel attenuation in the left main (LMA) and the proximal right coronary artery (RCA) were measured and correlated with differences in quantifications of stenosis grade between QCA and CTCA. A total of 113 coronary stenoses were detected by both methods (94 significant and 19 non-significant); 52 stenoses were rated as non-calcified and 61 as calcified lesions. The mean difference between QCA and quantitative CTCA grading was  $5.1 \pm 16.9\%$  (range –27 to 46%) overall;  $1.9 \pm 14.2\%$  (range –27 to 38%) for non-calcified lesions and  $7.8 \pm 18.6\%$  (range –23 to 46%) for calcified lesions. Mean vessel attenuation was  $362 \pm 76$  HU (range 191–584 HU) in the LMA and  $333 \pm 81$  HU (range 162–564 HU) in the RCA. Attenuation did not significantly correlate with differences in QCA and CTCA gradings, neither overall nor for calcified or non-calcified lesions. When 64-slice CTCA is used, coronary vessel attenuation had no impact on the quantitative grading of stenoses.

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64-slice CT has been shown to reliably detect significant coronary artery disease (CAD) [1–11]. For clinical decision-making, exact quantification of lesion severity can be important [12]. However, the quantification of coronary artery stenoses by CT coronary angiography (CTCA) is subjected to relatively large limits of agreement compared to the clinical reference standard, quantitative coronary angiography (QCA) [2, 3, 13–15]. It has been hypothesised that coronary vessel attenuation affects the accuracy of quantitative CTCA [16–18]. Several factors related to the contrast material regimen, such as the type and iodine concentration of the contrast material [18], the technique for bolus timing [17], and the injection volume and rate [19], have been shown to affect the attenuation of coronary arteries. Furthermore, current CTCA protocols [1–11] do not adapt to the individual patient's body mass index or to the individual's cardiac output, although these parameters may contribute to vessel attenuation [20–23]. As a consequence, attenuation in CTCA has been shown to vary strongly [17, 18, 22, 23] and the ideal attenuation remains undefined.

The purpose of this study was to determine the impact of vessel attenuation on quantitative CTCA.

## Methods and materials

### Patients

A total of 100 consecutive patients (42 women and 58 men; mean age  $64.4 \pm 9.4$  years; age range 39–87 years; mean body mass index (BMI)  $22.0 \pm 3.5$ ; BMI range 12.8–31.4) underwent QCA and CTCA and were prospectively enrolled in the present study. Both examinations were obtained for other reasons, as mentioned later, and not specifically for evaluation of vessel attenuation. 74 patients were suspected of having CAD, and had been referred to QCA on the basis of symptoms such as dyspnoea ( $n=17$ ), typical angina pectoris ( $n=27$ ), atypical chest pain ( $n=18$ ), or without symptoms to rule out CAD preoperatively ( $n=12$ ). The remaining patients ( $n=26$ ) had a history of known CAD with recurrent angina. Exclusion criteria for CTCA were hypersensitivity to iodinated contrast agent, renal insufficiency (creatinine levels  $>150 \mu\text{mol l}^{-1}$ ), non-sinus rhythm or haemodynamic instability.

The local ethics committee approved the study protocol and all patients gave written informed consent.

### CT data acquisition and post-processing

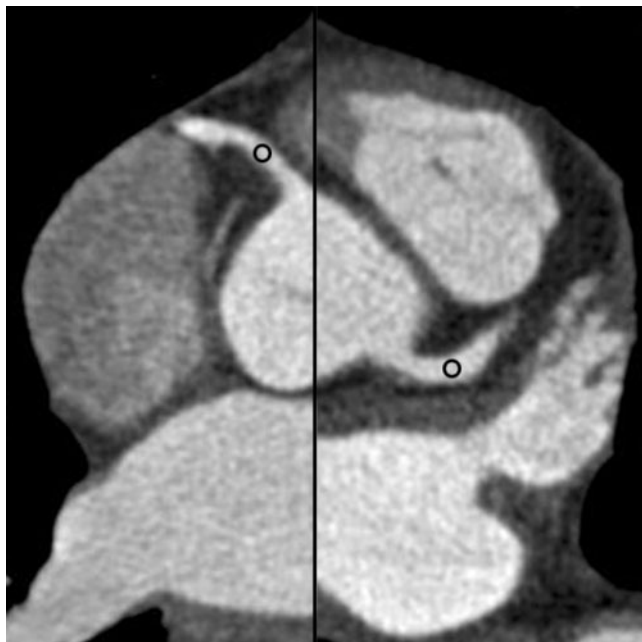
CT examinations were performed on a 64-slice CT scanner (Somatom Sensation 64, Siemens Medical

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Solutions, Forchheim, Germany). If necessary, intravenous metoprolol (5–20 mg) (Beloc, AstraZeneca, Zug, Switzerland) was administered prior to the CT examination to achieve a target heart rate of <70 beats per minute (bpm). In the presence of contraindications for  $\beta$ -adrenoreceptor antagonists or when the maximum dose did not lower the heart rate satisfactorily, the scan was performed even at higher heart rates. In addition, all patients received a single dose of 2.5 mg of isosorbiddinitrate sublingually (Isoket, Schwarz Pharma, Monheim, Germany) 2 min prior to the scan. The CTCA scan was started by continuously injecting a bolus of 80 ml of iodixanol (Visipaque 320, 320 mg ml<sup>-1</sup>, GE Healthcare, Buckinghamshire, UK) followed by 30 ml of saline solution into an antecubital vein via an 18-gauge catheter (injection rate 5 ml s<sup>-1</sup>). Bolus tracking was performed with a region of interest (ROI) in the ascending aorta, and image acquisition was automatically started 5 s after the signal attenuation reached a predefined threshold of 100 Hounsfield units (HU). Scanning was performed from 1 cm below the level of the tracheal bifurcation to the diaphragm in a cranio-caudal direction using the following scanning parameters: detector collimation 32 × 0.6 mm, slice collimation 64 × 0.6 mm by means of a z-flying focal spot, gantry rotation time 330 ms, pitch 0.2, tube potential 120 kV, and tube current × time product 650 effective mAs.

### CT image reconstruction and analysis

Data sets were retrospectively reconstructed throughout the entire cardiac cycle in 5% steps of the R–R interval. The adaptive cardio volume approach was used



**Figure 1.** Axial CT coronary angiography sections illustrating placement of the regions of interest (black circles) in the proximal right coronary artery and in the left main artery. Regions were defined as large as possible, at the same time avoiding partial volume effects and the inclusion of calcifications, plaques and stenoses.

for image reconstruction [24]. Reconstruction of axial images was performed with a slice thickness of 1.0 mm and an increment of 0.8 mm. All images were reconstructed using a medium-soft and a sharp tissue convolution kernel (B30f and B46f, the latter for the evaluation of calcified lesions) [25] and were transferred to an external workstation (Leonardo, Siemens Medical Solutions).

Coronary arteries were segmented as suggested by the American Heart Association [26]: the right coronary artery (RCA) was defined to include segments 1–4, the left main artery (LMA) to include segment 5, the left anterior descending artery (LAD) to include segments 6–10, and the left circumflex artery (LCX) to include segments 11–15. The intermedial artery, if present on the reconstruction, was designated as segment 16. Segments with a diameter of at least 1.5 mm at their origin were included. Diameter measurements were performed with an electronic caliper tool. All segments distal to an occluded vessel were excluded from analysis.

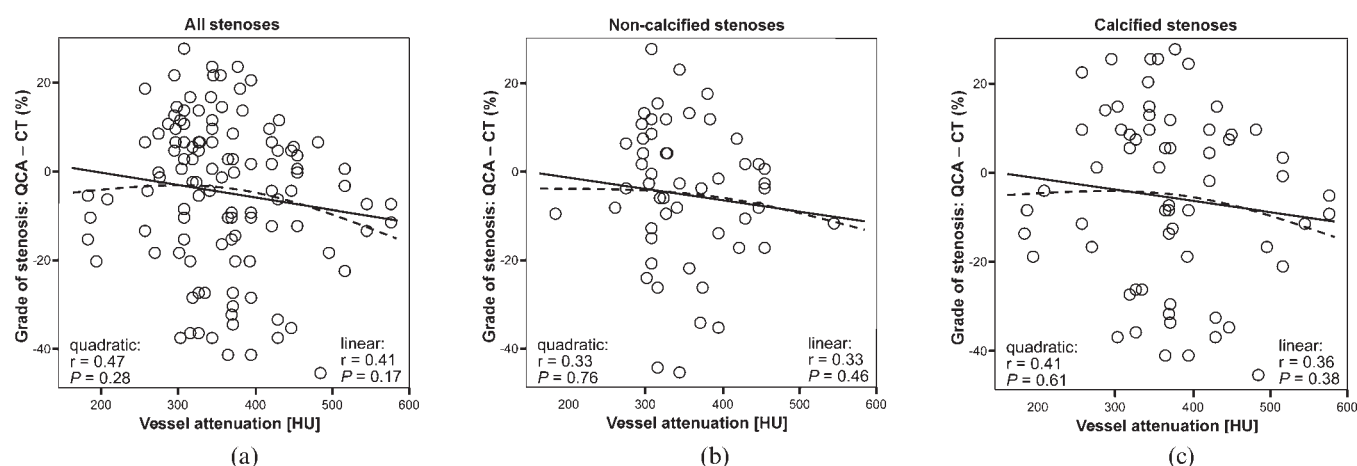
Images were evaluated in the best reconstruction interval and classified by two independent readers using axial source images, multiplanar reformations, and thin-slab maximum intensity projections on a per-segment basis. Both readers assessed all coronary artery segments for the presence of significant stenoses, which were defined as narrowing of the coronary luminal diameter by  $\geq 50\%$ . Furthermore, the degree of coronary stenosis was quantified. This was achieved by measuring vessel diameters with an electronic caliper tool on reconstructions perpendicularly oriented to the vessel course at the site of maximal luminal stenosis and in a reference vessel (results were rounded up or down to the nearest first decimal place before consensus reading). In case of multiple lesions in one segment, the segment was classified by the worst lesion. For any disagreement in data analysis between the two observers that was larger than 10%, consensus agreement was achieved; for all other cases, the mean was calculated. In addition, coronary lesions on CTCA images were grouped into calcified lesions and non-calcified lesions by two experienced readers in consensus.

To determine the impact of vessel attenuation on stenosis grading by CTCA, all lesions not concordantly detected by both methods, all segments without stenosis, and all segments with total occlusions were excluded from analysis. Absolute differences in stenosis grade quantification between the two methods were calculated for all other lesions.

Measurements of vessel attenuation were performed in the proximal RCA and the LMA by one experienced reader, who drew ROIs as large as possible, carefully avoiding calcifications, plaques and stenoses (Figure 1).

### Quantitative invasive coronary angiography

QCA was performed according to standard techniques, and multiple views were stored on a CD-ROM. The angiograms were quantitatively evaluated using QCA software (Xcelera, PhilipsMedical Systems, The Netherlands) by two independent and experienced interventional cardiologists who were blinded to the results from CT coronary angiography; the contrast-filled



**Figure 2.** Impact of coronary attenuation on stenosis grade quantification. (a) Linear and quadratic regression plot of the difference between the grades of stenosis obtained by quantitative coronary angiography (QCA) and CT coronary angiography (CTCA) of all coronary stenoses ( $n=113$ ). (Differences in stenosis grade for all stenosis detected by both methods (except total occlusions) are plotted against vessel attenuation.) (b) Linear and quadratic regression plot of the difference of the grades of stenosis obtained by QCA and CTCA of all non-calcified coronary stenoses ( $n=52$ ) against vessel attenuation. (c) Linear and quadratic regression plot of the difference of the grades of stenosis obtained by QCA and CTCA of all calcified coronary stenoses ( $n=61$ ) against vessel attenuation. No significant correlations were detected.

angiography catheter was used as reference for calibration. Coronary artery segments were defined as described above [26], and analysis was performed in all vessels with a luminal diameter of at least 1.5 mm, excluding those vessels distal to complete occlusions. Each vessel segment was scored as being significantly stenosed, *i.e.* with a reduction in diameter of  $\geq 50\%$ .

### Statistical analysis

Statistical analysis was performed using SPSS software (SPSS 15.0, Chicago, IL). Quantitative variables were expressed as mean  $\pm$  standard deviation (if normally distributed) or median (25th, 75th percentiles) (if non-normally distributed); categorical variables were expressed as frequencies and percentages.

Pearson linear and quadratic correlation analysis was performed to evaluate the correlation of vessel attenuation in the RCA and the LMA with difference between the imaging modalities in stenosis grade quantification in right and left coronary segments. A  $p$ -value of  $<0.05$  was considered to indicate statistical significance.

Bland-Altman (BA) analysis was used to determine the level of interobserver agreement in quantifying lesions.

### Results

CTCA and QCA were successfully performed in all patients within  $5 \pm 12$  days. 58 patients (58%) were on oral beta-receptor blocking medication as part of their baseline medication, and additional intravenous metoprolol was administered in 9 patients prior to the CTCA examination. During CTCA scanning, the mean heart rate was  $62.7 \pm 9.1$  bpm (range 45–87 bpm), and the heart rate variability was  $4.7 \pm 6.2$  bpm (range 0.5–22.1 bpm).

In 100 patients, 1278 coronary artery segments were available for analysis; 137 segments were missing

because of anatomical variants, 96 segments had a diameter less than 1.5 mm at their origin, 17 segments were excluded because of severe motion artifacts, 31 segments were excluded because of previous stent implantations, and 41 segments were excluded because they were distal to an occluding stenosis.

QCA identified 146 coronary artery stenoses with a diameter narrowing of  $\geq 50\%$ , whereas CTCA detected 155 stenoses of  $\geq 50\%$ . Interobserver agreement for the quantification of stenosis severity by CTCA revealed a mean difference of 0.5% between the two readers (BA limits of agreement,  $-44.2$  to  $45.2\%$ ; consensus reading had to be performed for 85 stenoses). After exclusion of all lesions that were not detected by both methods, and all segments with total occlusions ( $n=16$ ), 113 coronary stenoses remained for further analysis (94  $\geq 50\%$  and 19  $< 50\%$ ). 52 of these lesions were rated as non-calcified (44  $\geq 50\%$  and 8  $< 50\%$ ) and 61 were rated as calcified (50  $\geq 50\%$  and 11  $< 50\%$ ). Mean differences between QCA and quantitative CTCA was  $5.1 \pm 16.9\%$  (range  $-27$  to  $46\%$ ) overall;  $1.9 \pm 14.2\%$  (range  $-27$  to  $38\%$ ) for non-calcified lesions and  $7.8 \pm 18.6\%$  (range  $-23$  to  $46\%$ ) for calcified lesions.

Mean attenuation was  $362 \pm 76$  HU (range 191–584 HU) in the LMA and  $333 \pm 81$  HU (range 162–564 HU) in the RCA. Vessel attenuation was not significantly correlated with the mean difference between QCA- and CTCA-obtained gradings of stenoses, neither overall nor for calcified or non-calcified lesions ( $p \geq 0.17$ ) (Figure 2).

### Discussion

Quantitative assessment of coronary stenoses has been shown to have relatively large limits of agreement when 16-slice CTCA [13, 14] and 64-slice CTCA are used [3, 27]. Coronary vessel attenuation is known to vary widely in different CTCA examinations [17, 18, 22, 23], and might affect the accuracy of stenosis quantification by



CTCA. In fact, greater coronary attenuation has been associated with improved diagnostic accuracy [28]. To date, however, the impact of attenuation on the performance of quantitative CTCA has not been systematically evaluated.

In the present study, we found no significant effect of vessel attenuation on the quantitative grading of coronary artery stenoses by 64-slice CT.

Attenuation in *ex vivo* CTCA has been shown to influence attenuation measurements in coronary stenoses, *i.e.* high attenuation in the vessel causes a greater attenuation in calcified and non-calcified plaques [29]. From the images presented by Cademartiri et al [29], it appears reasonable to assume that vessel attenuation might affect the quantitative grading of stenoses, as high attenuation would lead to an underestimation of plaque size, specifically if the plaque is non-calcified. However, our study was not able to prove such direct interdependencies. This is most probably attributable, at least in part, to fundamental limitations of both techniques, CTCA and QCA.

During QCA, coronary stenoses are usually depicted from two orthogonal planar projections, allowing most lesions to be accurately reflected. Because of foreshortening, overlapping side branches or disease at bifurcation sites, two orthogonal views are occasionally unobtainable. Furthermore, certain complex luminal shapes cannot be accurately depicted with any arbitrary angle of view [30], which may have led to discrepancies between QCA grading of lesion severity and post-mortem evaluation [31, 32].

CTCA, on the other hand, acquires a three-dimensional data set, allowing image reconstructions at any desirable plane [33], and thereby overcomes the shortcomings of two-dimensional projections [34]. CTCA however provides lower spatial (and temporal) resolution when compared to QCA, which is likely to lead to unclear definition of coronary lesions and consecutive quantification errors.

Our study was performed using 64-slice CT rather than the most recent dual-source CT scanner technology [35]. We acknowledge that the limitations inherent to 64-slice CTCA and QCA mentioned above could have influenced our results. Within the range of vessel attenuation that occurred in our patients (191–584 HU), however, there was no impact of vessel attenuation on lesion quantification when CTCA and QCA were compared directly.

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